Remarks/Arguments

In the office action of July 30, 2007, claims 41-60 were rejected as a Final Office Action. Applicant traverses the finality of the rejection and respectfully requests its withdrawal as a final rejection. Applicants made a bona fide attempt to move prosecution forward through the drafting of new claims to directly address the grounds for rejection and filed their request for continuing examination. As such, this should be a first office action.

The claims stand rejected as follows:

1. Claims 41-60 stand rejected under 35 U.S.C. §112, first paragraph, written description;
2. Claims 41-60 stand rejected under 35 U.S.C. §112, second paragraph, and
3. Claims 41-60 stand rejected under 35 U.S.C. §102.

The Advisory Action mailed indicates that a new search would be required due to the new language added to claim 41. Claim 41 has been amended and the Examiner is directed to the Summary of the Invention for direct support for the language used in new Claim 41.

Claims 41-60 are rejected under 35 U.S.C. §112, first paragraph, written description.

Applicant traverses the rejection. However, the Applicant has amended the claims to address each and every ground for rejection and provides the following support for the claim amendments. Support for the term Type I collagen is found throughout the specification, however, the Applicant points specifically to paragraph [0022] to support that which is well known by the skilled artisan, that the Type I collagen is a protein that is a triple helix made from three proteins, two α1(I) chains and one α2(I) chain. Attached hereto is a copy of the section on Collagen from the Encyclopedia of Polymer Science and Engineering, Volume 3, Second Edition (1985), John Wiley and Sons (attached hereto as Appendix A), which outlines that which is well-known in the art.

The action rejects the use of the term "in vitro" and "conditions" in the claims as not having support in the specification. However, the exact recitation of the terms in the specification is not the legal standard for a 35 U.S.C. §112, first paragraph, written description. The standard is that:

> *Ipsis verbis* disclosure is not necessary to satisfy the written description requirement of section 112. Instead, the disclosure need only reasonably convey to persons skilled in the art that the inventor had possession of the

subject matter in question.

Fujikawa v. Wattanasin, 93 F. 3d 1559, 39 USPQ2d 1895 (Fed. Cir. 1996).

Applicant traverses this rejection and points the office to paragraph [0033], which clearly supports both the in vitro manufacture of the patch, but also conditions under which the Type I collagen is assembled and the cells are grown. Even a minimally skilled artisan would be able to make and use as well as understand the metes and bound of the present invention based solely on paragraph [0033]. However, the skilled artisan need not rely solely on paragraph [0033], the specification includes eighteen (18) specific examples of written description for the types of cells, tissue culture conditions, and sources for the Type I collagen that may be used with the present invention as claimed. Applicant has made a bona fide, good faith effort to resolve the remaining issues to move prosecution forward in the case and respectfully requests the office to provide guidance to the Applicant as regards acceptable claim language.

Applicant has addressed each and every ground for rejection and respectfully requests withdrawal of the rejections under 35 §112, first paragraph, written description.

Claims 41-60 are rejected under 35 U.S.C. §112, second paragraph, failure to particularly point out and distinctly claim.

Claims 41-60, at rejected for failure to support: (1) a recitation ("condition," which has been addressed *supra*); (2) omitting steps such as mixing a human cell and "other elements" (claims 41-60); and (3) omitting essential structural cooperation between elements (claims 48, 58, which have been amended to address the rejection). Applicant not only traverses the rejection, but fails to understand the nature of the rejection as regards the "omitted steps".

Briefly, the present invention provides for a simple, one step method of making a patch with anti-adhesive properties that is made by providing human cells under tissue culture conditions Type I collagen, which the cells form into a patch *in vitro*. If the office is requesting that the method include more that one step, which is not a requirement under the law or the rules of patent procedure, the Applicant respectfully requests guidance from the office as regards this requirement. Applicant believes that nothing is omitted from the claims as drafted. In order to move prosecution forward, Applicant also points to the dependent claims (which also stand rejected based on this requirement), which include additional steps, e.g., removal of the cells upon formation of the patch. Guidance from the office as to which

steps or elements the office believes are omitted is respectfully requested, or withdrawal of the rejection is also respectfully requested.

Claims 41-60 are rejected under 35 U.S.C. §102 as anticipated by US 5,700,688 ('688 patent).

The action takes the position that the claims 41-60 are anticipated by the '688 patent arguing that it discloses a tissue equivalent material formed from collagen Type I and III mixed with human fibroblasts. Applicant traverses the rejection as shows as follows.

Several reasons distinguish the present invention from that disclosed by Lee, et al., in the '688 patent. The '688 patent, and the other patents that are related thereto, are directed to making a uniform oriented tissue-equivalent that includes living cells. Stated another way, the '688 matrix is an oriented collagen and cell matrix. Furthermore, the materials manufactured by the '688 patent are manufactured to attach or adhere to body tissues, viz., injured ligaments, tendons and attachment to skeletal or cardiac muscle. Furthermore, the uniform oriented tissue-equivalent also includes other "proteinaceous" fibers.

As stated in the first paragraph of the Detailed Description of the Invention of the '688 patent (reproduced below), the collagen is formed in vitro "with living cells" and proteinaceous fibers. Together, these three components are then "oriented" into a "uniform oriented tissue-equivalent."

> **DETAILED DESCRIPTION OF THE INVENTION**
>
> **An oriented tissue-equivalent is defined herein as a material which is formed in vitro with living cells and proteinaceous fibers, is untaxially aligned (e.g., to thereby increase mechanical strength along the alignment axis), and has mechanical and physiological properties similar to in vivo oriented tissue.**

'688 Patent, Col. 4.

This uniform oriented tissue-equivalent is formed between two posts *in vitro* to achieve a matrix that is "stiffened" along the axis of two posts around which the collagen is formed, e.g., into a ligament or other structural tissue requiring high tensile strength. In particular, the method for making the uniform oriented tissue-equivalent of the '688 patent is summarized as follows,

(1986). As cells exert traction on the collagen matrix, the matrix becomes consolidated in the unconstrained axes. However, along the axis between the two rigid posts, the cells align the matrix which stiffens, and provides cells an orientation cue. In the periphery of the oriented tissue-equivalent, cell alignment is not observed due to relatively unrestrained matrix compaction in all dimensions. In the center of the oriented tissue-equivalent, where matrix compaction is rigidly constrained along one axis, uniform cell alignment is observed. These results suggest that to obtain a uniform oriented tissue-equivalent, the initial diameter of the reconstituted collagen gel should be small relative to the distance between the two posts.

'688 patent, Col. 6.

In other words, the '688 patent teaches a contracted or rigid structure that is oriented along the axis formed by the two posts. The uniform oriented tissue-equivalent of the '688 patent is "rigidly constrained along one axis"... in which uniform cell alignment is observed Figure 8 of the'688 patent is described as a "gel [that] is constrained in the circumferential direction by the two fixed posts, and collagen fibers should be oriented in that direction. Col. 8, ll. 40-42. The constraint of manufacture of the '688 patent is furthered by cross-linking of the collagen, as taught in Example V ('688 patent, Col. 18).

In the Summary of the Invention, the '688 applicants correlate alignment of the strands with the strength

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for cell alignment. The connective tissue cells align along the defined axis to produce an oriented tissue-equivalent having increased mechanical strength in the direction of the axis.

('688 patent, Col. 3).

In contrast to the '688 patent, the patch of the present invention is not oriented and is preferably is not constrained during manufacture, nor does it require additional proteinaceous fibers or crosslinking. Furthermore, the patch of the present invention more closely resembles natural collagen formed by cellular monolayer of fibroblasts because the matrix is oriented by the fibroblasts as it would be in vivo, and not constrained as taught by the '688 patent. Furthermore, the fibroblasts of the present invention are not seeded "into" the collagen and then tensed between two posts to form the uniform oriented tissue-equivalent.

> The oriented tissue-equivalent of the present invention can be used to replace damaged connective tissue, for example ligaments, tendons, skeletal and cardial muscle, and has several advantages over nonliving artificial materials. Unlike nonliving synthetic materials which provide a poor surface for immune cells to adhere, the oriented tissue-equivalent is accessible to and can be protected by the immune system. The oriented tissue-equivalent is a living tissue, thus having the ability to respond to physiological demands and to repair itself. Further, integration of the oriented tissue-equivalent with the host tissue improves with time.

('688 patent, Col. 3).

In addition to the lack of anticipation, using the teachings of the '688 patent provide no expectation of success in the formation of the anti-adhesive patch made using the present invention. Several reasons support the argument for a failure to expect success. First, the skilled artisan having the '688 patent would seed the collagen with cells to form the uniform oriented tissue-equivalent under conditions that would align the strands and the cells and molded into a high tensile strength tissue, as measured in the mechanical apparatus claimed in the '688 patent. Second, the skilled artisan would incubate the cells for at least 42 days to achieve the uniform oriented tissue-equivalent. The present invention includes no such requirement. Third, the skilled artisan seeking a non-adhesive patch would not cross-link the collagen to increase its tensile strength due to increases in immune recognition and immunogenicity of the patch, as taught in Example V.

The physical difference between the '688 patent and the present invention is readily apparent by comparing Figure 5 of the '688 patent and Figure 2A of the present invention. In Figure 5 of the '688 patent, the alignment of the cells in the matrix is in sharp contrast with Figure 2A of the present invention, in which the cells are not aligned along any axis, nor do they provide mechanical strength to the matrix.

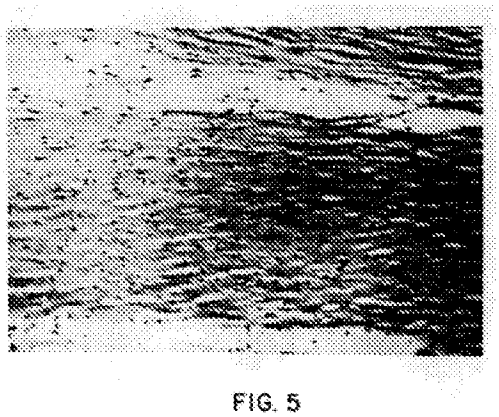


FIG. 5

Figure 5 '688 Patent

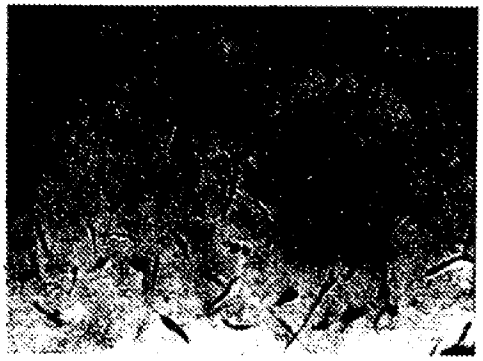
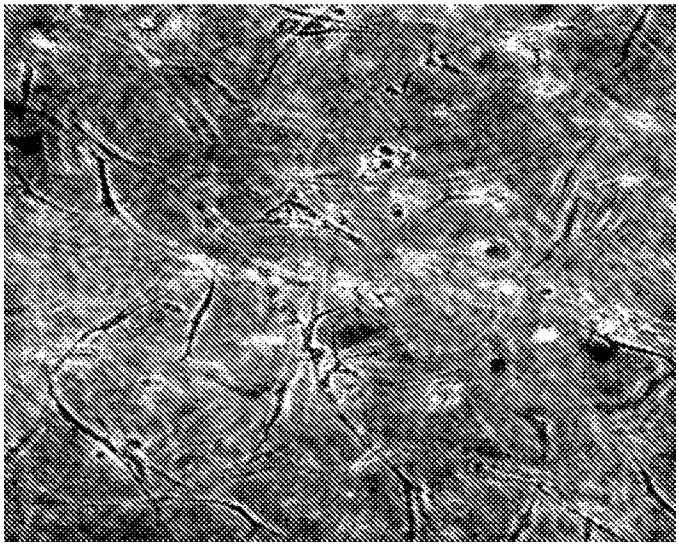


Fig. 2a

Figure 2A, present invention

Below is a better image of the three-dimensional, non uniform, non directional matrix formed using of the present invention that is in sharp contrast with Fig. 5 of the '688 patent.



This figure shows the random cell distribution of the patch of the present invention. Because the patch is 3-dimensional and the cells are distributed in the matrix in three dimensions and the focus of the microscope objective is in one plane some cells are blurred and are out of focus.

In the '688 patent, the cell and matrix alignment is critical to the physical strength for the use of the uniform oriented tissue-equivalent. To achieve that physical strength, the cells and matrix must be incubated for at least 28 days before the increase in mechanical strength (see Figures 9, 10, 12). The present invention requires no such mechanical force to form the patch and is, in fact, completed within a 10-14 day period (see Figures 3B and 4B and Example 11).

Therefore, the '688 patent does not anticipate or render obvious the present invention. Applicant believes that claims 41-60 as amended overcome the rejection based on the art of record. Applicant respectfully requests allowance of all the claims.

Conclusion

In light of the remarks and arguments presented above, Applicant respectfully submits that the claims in the Application are in condition for allowance. Favorable consideration and allowance of the pending claims is therefore respectfully requested.

If the Examiner has any questions or comments, or if further clarification is required, it is requested that the Examiner contact the undersigned at the telephone number listed below.

Dated: December 31, 2007

Respectfully submitted,
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